

Remarks

Claims 24, 28, 37, and 39-40 have been amended without any intention of disclaiming equivalents thereof. Claims 25 and 38 have been cancelled without prejudice to their subsequent reintroduction into this application or their introduction into a related application. Claims 105 and 106 have been added. Upon entry of this paper, claims 24, 26-37, 39-48, and 104-106 will be pending and under consideration.

Applicants have amended independent claims 24 and 37 to incorporate the elements of claims 25 and 38, respectively, to recite a template *associated with a capturable moiety*. Support for this amendment may be found throughout the application as filed, for example, in claims 25 and 38 of the application as filed. Applicants have canceled claims 25 and 38 and amended the dependencies of claims 28 and 39-40 accordingly. In addition, Applicants have added new claims 105 and 106. New claim 105 incorporates the elements of independent claim 24 and dependent claims 34 and 35. New claim 106 incorporates the elements of independent claim 37 and dependent claims 44 and 46. Accordingly, support for these new claims can be found, for example, in the original corresponding claims from which they are derived. Applicants believe that the aforementioned amendments introduce no new matter. The outstanding rejections are addressed in the order in which they appear in the Office Action.

Double Patenting Rejections

According to sections 2-5 of the outstanding Office Action, certain claims presently stand rejected under the judicially created doctrine of obviousness-type double patenting in view of certain claims in U.S. Patent Number 7,070,928 in view of Sergeev; provisionally stand rejected in view of certain claims in U.S. Patent Application Serial No. 11/586,851; and provisionally stand rejected in view of certain claims in U.S. Patent Application Serial No. 10/949,163. Applicants respectfully request that these rejections be held in abeyance until allowable subject matter has been determined in this case. Once allowable subject matter has been identified, Applicants intend to file a Terminal Disclaimer, if appropriate.

Examiner's Claim Interpretation

According to the *Claim Interpretation* section on page 6 of the Office Action, the Examiner has indicated that the term 'reactive unit' is being given the broadest reasonable interpretation in light of the specification and interprets the term to encompass "nucleic acid templated synthesis techniques which include ligation reactions between nucleotides." Applicants attempted to address this issue in Applicants' arguments filed December 22, 2006, in which Applicants amended independent claims 24 and 37 to clarify that the reaction product is not a nucleic acid. Applicants invite the Examiner to contact the undersigned regarding any outstanding matters related to this issue.

Rejection Under 35 U.S.C. § 103

According to pages 7-15 of the outstanding Office Action, claims 24-48 and 104 presently stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Sergeev, WO 00/61775 ("Sergeev") in view of Gartner and Liu (2001) Journal of the American Chemical Society 123: 6961-63 ("Gartner"). Applicants respectfully traverse this obviousness rejection to the extent that it is maintained over the claims, as amended, in view of the following comments.

The standard for determining obviousness is described in the Supreme Court's recent decision in *KSR v. Teleflex*. Applicants emphasize that 35 U.S.C. §103 requires that the subject matter, taken as a whole, must be considered when evaluating the patentability of an invention.

Applicants respectfully submit that Sergeev and Gartner, alone or in combination, fail to teach or suggest a *template associated with a capturable moiety*, as is required by independent claims 24 and 37 as amended, and claims depending therefrom. Sergeev discloses a method of synthesizing biologically active compounds directly in the cells of living organisms. See page 10, lines 22-27. Sergeev achieves this by hybridizing two or more oligomers, each bound to a precursor of a biologically active compound, to cellular RNA or DNA within a cell. *Id.* When the oligomer-precursors hybridize to specific RNA or DNA sequences within the cell, the biologically inactive precursors interact with one another to make a biologically active form of the compound. See, for example, Figure 1. The purpose of Sergeev appears to be to deliver a biologically active compound only to those cells where the specific RNA or DNA is produced.

See page 3, lines 5-9. Accordingly, Applicants submit that there is no teaching or suggestion in Sergeev to attach a capturable moiety to the template (e.g. cellular RNA or DNA).

Gartner also fails to teach or suggest a *template associated with a capturable moiety*. At best, Gartner describes a capturable moiety (e.g. biotin) associated with a reactive group, not with a template. See, for example, Figure 6. The Office indicates that Gartner teaches an embodiment wherein the template is associated with a capturable moiety and refers to Figure 6 of Gartner. See page 13, paragraph 3 of the Office Action. Applicants respectfully submit that Figure 6 clearly shows that the capturable moiety is associated with the transfer unit, not with the template, both before and after the reaction. Since neither Sergeev nor Gartner teach or suggest a *template associated with a capturable moiety*, the combination of Sergeev and Gartner also fail to teach or suggest a *template associated with a capturable moiety*.

To the extent that this rejection applies to new claims 105 and 106 (which incorporate prior claims 24, 34 and 35, and claims 37, 44 and 46, respectively), Applicants respectfully traverse the rejection. Specifically, Applicants respectfully submit that Sergeev and Gartner, alone or in combination, fail to teach or suggest an *in vitro* method wherein the non-enhanced reaction in step (b) is incompatible with the enhanced reaction in step (b).

To explain, the nucleic acid-templated synthesis of the present invention permits one-pot diversification of synthetic library precursors into products of multiple reaction types, even though some of the reactive units are incompatible, for example, where a reaction between the second and third reactive units is incompatible with a reaction between the second and first reactive units. Example 7 of the present invention demonstrates that oligonucleotides can simultaneously direct several different synthetic reaction types within the same solution, even though the reactants involved are otherwise cross-reactive. These findings also demonstrate that it is possible to perform a one-pot diversification of synthetic library precursors into products using multiple, simultaneous and not necessarily compatible reaction types.

Sergeev fails to teach or suggest at least this element of claims 105 and 106. Specifically, in Sergeev's Figures and pages that describe three or more reactive units (Figures 8-10 and pages 15-17) the reactive units are peptides, as in Figures 8 and 9, or oligoribonucleotides as in Figure

10. Each peptide or oligoribonucleotide is attached to an oligonucleotide that hybridizes to the cellular DNA or RNA. After hybridization, the spatially adjacent peptides or oligoribonucleotides bond to form protein or RNA, respectively. As shown in Figure 8, the first reactive group (e.g. peptide 1) bonds with the second reactive group (e.g. peptide 2), which bonds with the third reactive group (peptide 3). Since it is necessary for Sergeev's second reactive group to bond with both the first and third reactive groups (to form protein or RNA), the reaction between the second and first reactive units must be compatible with the reaction between the second and third reaction units. However, this is contrary to the requirement of claims 105 and 106 that those reactions are incompatible. The Office indicates that Sergeev's Figure 4 also applies to this element of Applicants' claims 105 and 106. See Office Action page 10, paragraph 3, and page 11, paragraph 3. However, Applicants respectfully submit that Sergeev's Figure 4 describes only two reactive units, identified as precursors A and B on page 22.

Gartner also fails to teach or suggest this element of claims 105 and 106. Specifically, the experiment described in Figure 6 of Gartner employs only two reactive units. The first is maleimide, linked to the templates, and the second is thiol, linked to the reagents. Accordingly, the experiment described in Figure 6 does not contain a third reactive unit. Moreover, Figure 7 suggests that the hybridization of the first transfer unit (e.g. reagent 1 library) and the hybridization of the second transfer unit (e.g. next reagent library) are performed sequentially, so it does not address the issue of incompatible reactions in the same pot. Accordingly since neither Sergeev nor Gartner teach or suggest an *in vitro* method wherein the non-enhanced reaction in step (b) is incompatible with the enhanced reaction in step (b), they do not teach this element in combination.

Alternatively, Applicants submit that modification of Sergeev in accordance with Gartner substantially changes the function of Sergeev's invention and renders Sergeev unsatisfactory for its intended purpose. In its recent decision in *KSR v. Teleflex*, the Supreme Court reaffirmed the *Graham* factors in the determination of obviousness under 35 U.S.C. § 103(a) and reiterated that a "patent for a combination which only unites old elements with no change in their respective functions . . . obviously withdraws what is already known into the field of its monopoly and

diminishes the resources available to skillful men." *Citing* Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U. S. 147, 152 (1950). Moreover, it is well accepted that if a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). As noted above, the purpose of Sergeev appears to be to deliver a biologically active compound only to those cells where the specific RNA or DNA is produced. See page 3, lines 5-9. Accordingly, modification of Sergeev to address the deficiencies in its description would require, at least, that one skilled attach a capturable moiety to the template (e.g. the cellular DNA or RNA). Applicants respectfully submit that modification of Sergeev in this manner changes the function of Sergeev and renders Sergeev unsatisfactory for its intended purpose, in contradiction to the recent decision in *KSR v. Teleflex*.

Because, when taken as a whole, Sergeev and Gartner, alone in combination, fail to teach or suggest at least the above-identified elements of independent claims 24, 37, 105, and 106, as amended, and the claims depending therefrom, Applicants respectfully request that the rejection as applied to these claims be reconsidered and withdrawn. Alternatively, because modifying Sergeev would substantially change the function of Sergeev's invention and render Sergeev unsatisfactory for its intended purpose, in contradiction to current law, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 102(b)

According to page 15-21 of the outstanding Office Action, claims 24, 30-34, 36-37, 41-45, 47-48, and 104 presently stand rejected under 35 U.S.C. § 102(b) as anticipated by Dorner *et al.* (1984) ("Dorner"). Without acquiescing to this rejection, but in order to promote prosecution, Applicants have amended independent claims 24 and 37 to incorporate the elements of claims 25 and 38, respectively. Since the Office Action has indicated that this rejection is not applicable to claims 25 and 38, the rejection should now be moot as applied to claims 24 and 37, as amended, and all claims depending therefrom.

Similarly, Applicants have introduced new claims 105 and 106. Claim 105 incorporates the elements of independent claim 24 and dependent claims 34 and 35. Claim 106 incorporates the elements of independent claim 37 and dependent claims 44 and 46. Since the Office Action has indicated that this rejection is not applicable to claims 35 and 46, this rejection should not apply to new claims 105 and 106.

Because Dorner fails to teach or suggest each and every element of independent claims 24 and 37, and new claims 105 and 106, and all claims depending therefrom, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Conclusion

Applicants believe that, in the view of the above amendments and comments, the pending claims are in condition for allowance. Early favorable action is respectfully solicited. The Office is invited to contact the undersigned with any questions about this submission.

Respectfully submitted,

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